

<p align="center">Advisory Action Before the Filing of an Appeal Brief</p>	Application No. 10/731,256	Applicant(s) MACDONALD ET AL.	
	Examiner Nathan W. Schlientz	Art Unit 1616	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 05 December 2008 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.
b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
(a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
(b) ☐ They raise the issue of new matter (see NOTE below);
(c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
(d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☐ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
The status of the claim(s) is (or will be) as follows:
Claim(s) allowed: _____.
Claim(s) objected to: _____.
Claim(s) rejected: _____.
Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because:
See Continuation Sheet.
12. ☐ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). _____.
13. ☐ Other: _____.

Notice of References Cited attached

/John Pak/
Primary Examiner, Art Unit 1616

Continuation of 11. does NOT place the application in condition for allowance because:
As requested, a copy of Daraio et al. is supplied for Applicant's records.

Applicant's Remarks filed 05 December 2008 have been fully considered but they are not persuasive.

35 U.S.C. 112

Applicants argue on page 6 that one of ordinary skill in the art would reasonably conclude that a pH altering material could be an acid or a base. However, the instant specification does not state anywhere that pH altering materials include acids and bases. Therefore, there is not support for this in the claims.

35 U.S.C. 103

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Rejection of claims 28, 30, 31, 33-35, 37, 38, 40, 42-44, 46, 64 and 65 over Bosch et al., Breitbarth, and Ma et al., as evidenced by Daraio et al.

Applicants argue on page 7 that one of ordinary skill in the art would not look to the hair growth teaching of Breitbarth to construct Applicant's invention. However, the examiner respectfully argues that Breitbarth is cited to show the state of the art at the time of the instant invention. Breitbarth teaches that administering drugs attached to the surface of particles that are then readily and controllably released as a function of pH was well-known and extensively used at the time of the instant invention (col. 5, ln. 11-19).

Applicants further argue on page 8 that the Nalco particles used by Bosch et al. comprise an alumina core, and not silica coated with alumina. However, the examiner respectfully argues that when Bosch et al. refer to the Nalco alumina core, they are referring to the particles without the active agent bound to the surface. Also, Bosch et al. specifically teaches the use of other silica coated alumina particles in Example 2 (Ludox CL are 12 nm alumina coated silica). Therefore, Bosch et al. teach the use of alumina coated silica particles for binding active agents.

Applicants also argue on page 9 that Ma et al. is directed to absorption of proteins and antibiotics on alumina membranes during filtration, and simply indicates that the amount adsorbed is dependent upon pH. Applicants claim a functional compound bonded to the surface of nanoparticles and the release upon exposure to a pH change. However, the examiner respectfully points out that the instant claims do not differentiate the type of bonding between particles and the functional compound, and would include adsorption. The examiner further argues that Ma et al. teach that changes in pH will affect the binding of tetracycline to alumina, wherein a change in pH of either acidic or basic change results in a release of tetracycline.

Rejection of claims 28, 30, 31, 33-35, 37, 38, 40, 42-44, 46, 64 and 65 over Tan et al. in view of Bosch et al., Breitbarth and Ma et al., as evidenced by Daraio et al.

Applicants argue on page 10 that Tan et al. do not disclose or suggest the claimed alumina-coated silica nanoparticles. However, the examiner respectfully argues that Tan et al. reasonably teach nanoparticles wherein silica is coated with another layer, wherein active agents are bound to the surface of the nanoparticles. Bosch et al. reasonably teaches nanoparticles comprising silica coated with alumina for attaching active agents. Breitbarth et al. teach the release of actives from nanoparticles as a result of a change in pH is extensively used, and Ma et al. teach that tetracycline is released from alumina as a result in acidic or basic changes in pH.